ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Lokelma 5 g powder for oral suspension
Lokelma 10 g powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Lokelma 5 g powder for oral suspension
Each sachet contains 5 g sodium zirconium cyclosilicate

Lokelma 10 g powder for oral suspension
Each sachet contains 10 g sodium zirconium cyclosilicate

3. PHARMACEUTICAL FORM

Powder for oral suspension.

White, free flowing powder essentially free of debris and particulates.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Lokelma is indicated for the treatment of hyperkalaemia in adult patients (see section 4.4 and 5.1).

4.2 Posology and method of administration

Posology

Adults, including the elderly

Correction phase
The recommended starting dose of Lokelma is 10 g, administered three times a day orally as a suspension in water. When normokalaemia is achieved, the maintenance regimen should be followed (see below).

Typically, normokalaemia is achieved within 24 to 48 hours. If patients are still hyperkalaemic after 48 hours of treatment, the same regimen can be continued for an additional 24 hours. If normokalaemia is not achieved after 72 hours of treatment, other treatment approaches should be considered.

Maintenance phase
When normokalaemia has been achieved, the minimal effective dose of Lokelma to prevent recurrence of hyperkalaemia should be established. A starting dose of 5 g once daily is recommended, with possible titration up to 10 g once daily, or down to 5 g once every other day, as needed, to maintain a normal potassium level. No more than 10 g once daily should be used for maintenance therapy.

Serum potassium levels should be monitored periodically during treatment. Monitoring frequency

will depend upon a variety of factors including other medications, progression of chronic kidney disease and dietary potassium intake.

If severe hypokalaemia should occur Lokelma should be discontinued and the patient re-evaluated.

Missed dose
If a patient misses a dose they should be instructed to take the next usual dose at their normal time.

Special populations

Patients with renal/hepatic impairment
No changes from the normal doses are required for patients with renal or hepatic impairment.

Paediatric population
The safety and efficacy of Lokelma in children and adolescents (< 18 years) have not been established. No data are available.

Method of administration
For oral use.
The entire contents of the sachet should be emptied in a drinking glass containing approximately 45 ml of water, and stirred well. The powder will not dissolve. The tasteless liquid should be drunk while still cloudy. If the powder settles, the water should be stirred again. It should be ensured that all of the content is taken.
The suspension can be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance.

4.4 Special warnings and precautions for use

Serum potassium levels
Serum potassium should be monitored when clinically indicated, including after changes are made to medicinal products that affect the serum potassium concentration (e.g. renin-angiotensin-aldosterone system (RAAS) inhibitors or diuretics) and after the Lokelma dose is titrated.

Hypokalaemia
Hypokalaemia may be observed (see section 4.8). Dose titration as described under maintenance posology may be required in such cases to prevent moderate to severe hypokalaemia. In patients with severe hypokalaemia, Lokelma should be discontinued and the patient re-evaluated.

QT Prolongation
During correction of hyperkalaemia, a lengthening of the QT interval can be observed as the physiologic result of a decline in serum potassium concentration.

The risk of interaction with X-rays
Sodium zirconium cyclosilicate may be opaque to X-rays. If the patient is having abdominal X-rays, radiographers should keep this in mind.

Intestinal perforation
The risk for intestinal perforation with the use of Lokelma is currently unknown. No events of intestinal perforation have been reported with Lokelma. Since intestinal perforation has been reported with polymers that act in the gastrointestinal tract, specific attention should be paid to signs and symptoms related to intestinal perforation.

Limitations of the clinical data
Patients on dialysis
Lokelma has not been studied in patients receiving dialysis treatment.

Severe hyperkalaemia
There is limited experience in patients with serum potassium concentrations greater than 6.5 mmol/L.

Long-term exposure
Clinical trials with Lokelma have not included exposure longer than one year.

4.5 Interaction with other medicinal products and other forms of interaction

Effect of other medicinal products on sodium zirconium cyclosilicate
As sodium zirconium cyclosilicate is not absorbed or metabolised by the body, there are no expected effects of other medicinal products on its function.

Effect of sodium zirconium cyclosilicate on other medicinal products
As sodium zirconium cyclosilicate is not absorbed or metabolised by the body, there are limited effects on the function of or binding to other medicinal products. Sodium zirconium cyclosilicate can transiently increase gastric pH by absorbing hydrogen ions and can lead to changes in solubility and absorption kinetics for co-administered medicinal products with pH-dependent solubility. In a clinical drug-drug interaction study conducted in healthy subjects co-administration of amlodipine, clopidogrel, atorvastatin, furosemide, glipizide, warfarin, losartan, or levothyroxine did not result in clinically meaningful drug-drug interactions and no dose adjustments are required. Consistent with other gastric acid modifiers, dabigatran C_{max} and AUC values were approximately 40% lower when co-administered with sodium zirconium cyclosilicate, however, sodium zirconium cyclosilicate and dabigatran may be co-administered without adjusting the dose of dabigatran.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no data from the use of sodium zirconium cyclosilicate in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Lokelma during pregnancy.

Breast-feeding
In a postnatal study in rats, maternal exposure to sodium zirconium cyclosilicate had no effect on postnatal development. Due to its physicochemical properties, sodium zirconium cyclosilicate is not systemically absorbed and is not expected to be excreted in breast milk. No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to sodium zirconium cyclosilicate is negligible. Lokelma can be used during breast-feeding.

Fertility
There were no adverse effects on embryo-foetal development in treated rats or in rabbits.

4.7 Effects on ability to drive and use machines

Lokelma has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
The most commonly reported adverse reactions were hypokalaemia (2.3%) and oedema related events (5.7%).

Tabulated list of adverse reactions
The safety profile of Lokelma was evaluated in clinical trials involving 1760 patients with 430 patients exposed for one year.
The adverse reactions identified from controlled trials are shown in Table 1. The following convention was used for frequency of adverse reactions: Very common (≥ 1/10); Common (≥ 1/100 to < 1/10); Uncommon (≥ 1/1,000 to < 1/100); Rare (≥ 1/10,000 to < 1/1,000); Very rare (< 1/10,000), not known (cannot be estimated from the available data).

Table 1. List of adverse reactions in clinical studies

System Organ class	Common
Metabolism and nutrition disorders	Hypokalaemia
General disorders and administration site conditions	Oedema related events

Description of selected adverse reactions
Hypokalaemia
In clinical trials 2.3% of patients developed hypokalaemia with a serum potassium value less than 3.5 mmol/L, which was resolved with dose adjustment or discontinuation of Lokelma.

Oedema related events
Oedema related events, including fluid overload, fluid retention, generalised oedema, hypervolaemia, localised oedema, oedema, oedema peripheral, peripheral swelling, were reported by 5.7% of Lokelma patients. The events were observed in the maintenance phase only and were more commonly seen in patients treated with 15 g. Up to 53% were managed by initiating a diuretic or adjusting a diuretic dose; the remainder did not require treatment.

Long term exposure (interim data)
In an ongoing clinical trial with open-label exposure of Lokelma up to 1 year in 751 subjects, the following events were reported as related by investigators: gastrointestinal events (constipation, diarrhoea, abdominal pain/distension, nausea and vomiting); and hypersensitivity reactions (rash, pruritus, and dermatitis). A causal relationship between these events and Lokelma has not been finally established.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdose with sodium zirconium cyclosilicate could lead to hypokalaemia. Serum potassium should be checked and potassium supplemented as needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for treatment of hyperkalaemia and hyperphosphatemia,
ATC code: V03AE10

Mechanism of action
Sodium zirconium cyclosilicate is a non-absorbed, non-polymer inorganic powder with a uniform micropore structure that preferentially captures potassium in exchange for hydrogen and sodium

cations. Sodium zirconium cyclosilicate is highly selective for potassium ions, even in the presence of other cations such as calcium and magnesium, *in vitro*. Sodium zirconium cyclosilicate captures potassium throughout the entire gastrointestinal (GI) tract and reduces the concentration of free potassium in the GI lumen, thereby lowering serum potassium levels and increasing faecal potassium excretion to resolve hyperkalaemia.

Pharmacodynamic effects

Sodium zirconium cyclosilicate starts reducing serum potassium concentrations as soon as 1 hour after ingestion and normokalaemia can be achieved typically within 24 to 48 hours. Sodium zirconium cyclosilicate does not affect serum calcium or magnesium concentrations, or urinary sodium excretion. There is a close correlation between starting serum potassium levels and effect size; patients with higher starting serum potassium levels have greater reductions in serum potassium. There is a reduction in urinary potassium excretion which is a consequence of a reduction in serum potassium concentration. In a study of healthy subjects given Lokelma 5 g or 10 g once daily for four days, dose-dependent reduction in serum potassium concentration and total urinary potassium excretion were accompanied by mean increases in faecal potassium excretion. No statistically significant changes in urinary sodium excretion were observed.

There were no studies conducted to investigate the pharmacodynamics when sodium zirconium cyclosilicate is administered with or without food.

Sodium zirconium cyclosilicate has also been shown to bind ammonium *in vitro* and *in vivo*, thereby removing ammonium and increasing serum bicarbonate levels. Lokelma treated-patients experienced an increase of 1.1 mmol/L at 5 g once daily, 2.3 mmol/L at 10 g once daily, and 2.6 mmol/L at 15 g once daily in bicarbonate compared with a mean increase of 0.6 mmol/L for those receiving placebo. In an environment where other factors affecting renin and aldosterone were not controlled, Lokelma demonstrated a dose-independent reduction in mean serum aldosterone levels (range: -30% to -31%) compared with the placebo group (+14%). No consistent effect on systolic and diastolic blood pressure has been observed.

In addition, mean reductions in blood urea nitrogen (BUN) were observed in the 5 g (-1.1 mg/dL) and 10 g (-2.0 mg/dL) three times daily groups compared with small mean increases in the placebo (0.8 mg/dL) and low dose sodium zirconium cyclosilicate (0.3 mg/dL) groups.

Clinical efficacy and safety

The potassium-lowering effects of Lokelma have been demonstrated in three randomised, double-blind, placebo-controlled trials in patients with hyperkalaemia in association with chronic kidney disease (75% with estimated Glomerular Filtration Rate (eGFR) 4-60 mL/min/1.73 m^2), heart failure (40% NYHA I-IV), diabetes mellitus (61% Type 1-2) and use of RAAS inhibitors therapy (68%). All three studies tested the initial effect of Lokelma to correct hyperkalaemia during a 48-hour period and two studies also tested maintenance of normokalaemia effect obtained. In addition two open-label extension studies tested long-term safety of Lokelma. These five studies included 1760 patients given doses of Lokelma; 430 exposed for at least 360 days. In the studies, Lokelma reduced serum potassium and maintained normal serum potassium levels regardless of the underlying cause of hyperkalaemia, age, sex, race, comorbid disease or concomitant use of RAAS inhibitors. No dietary restrictions were imposed; patients were instructed to continue their usual diet without any specified alterations.

Study 1

A two-phase, placebo-controlled correction and maintenance use study

A two-part, double-blind, randomised, placebo-controlled clinical trial of 753 patients (mean age of 66 years, range 22 to 93 years) with hyperkalaemia (5 to ≤ 6.5 mmol/L, baseline potassium average 5.3 mmol/L), and included patients with chronic kidney disease, heart failure, diabetes mellitus and those on RAAS inhibitor therapy.

During the correction phase, patients were randomised to receive Lokelma (1.25 g, 2.5 g, 5 g or 10 g) or placebo, administered three times daily for the initial 48 hours (Table 2).

Table 2. Correction phase (Study 1): Percentage of normokalaemic subjects after 48 hours of Lokelma

		Lokelma dose (three times daily)			
	Placebo	**1.25 g**	**2.5 g**	**5 g**	**10 g**
N	158	154	141	157	143
Baseline serum potassium, mmol/L	5.3	5.4	5.4	5.3	5.3
Normokalaemic at 48 hours, %	48	51	68	78	86
p-value vs. placebo		NS	< 0.001	< 0.001	< 0.001

NS: not significant

Lokelma 10 g administered three times daily lowered serum potassium -0.7 mmol/L at 48 hours (p<0.001 vs. placebo); statistically significant 14% potassium reduction was observed 1 hour after the first dose. Patients with higher starting potassium levels had a greater response to Lokelma. Patients with pre-treatment potassium levels in excess of 5.5 mmol/L (average baseline 5.8 mmol/L) saw an average decrease of 1.1 mmol/L at 48 hours while those with starting potassium levels at or below 5.3 mmol/L had an average decrease of 0.6 mmol/L at the highest dose.

Patients who became normokalaemic after receiving Lokelma during the correction phase were re-randomised to receive once daily placebo or once daily Lokelma at the same dose level as they had received three times daily during the correction phase (Table 3).

Table 3. Maintenance phase (12 days, Study 1): Mean number of normokalaemic days

	Maintenance phase treatment (once daily)				
	Placebo		**Lokelma**		**P-value vs. placebo**
Correction phase Lokelma dose	**n**	**Days**	**n**	**Days**	
1.25 g three times daily	41	7.6	49	7.2	NS
2.5 g three times daily	46	6.2	54	8.6	0.008
5 g three times daily	68	6.0	64	9.0	0.001
10 g three times daily	61	8.2	63	10.2	0.005

NS: not significant

At the end of the maintenance period, when Lokelma was no longer administered, average potassium levels increased to near baseline levels.

Study 2
A multi-phase, placebo-controlled maintenance study with extension
In the correction phase of the study, 258 patients with hyperkalaemia (baseline average 5.6, range 4.1 - 7.2 mmol/L) received 10 g of Lokelma administered three times daily for 48 hours. Reductions in potassium were observed 1 hour after the first 10 g dose of Lokelma. Median time to normokalaemia was 2.2 hours with 66% of patients achieving normokalaemia at 24 hours and 88% at 48 hours. Responses were larger in patients with more severe hyperkalaemia; serum potassium fell 0.8, 1.2 and 1.5 mmol/L in patients with baseline serum potassium < 5.5, 5.5-5.9 and ≥ 6 mmol/L, respectively.

Patients who achieved normokalaemia (potassium levels between 3.5 and 5 mmol/L) were randomised in a double-blind fashion to one of three doses of Lokelma [5 g (n=45), 10 g (n=51), or 15 g (n=56)] or placebo (n=85) administered once daily for 28 days (the double-blind randomised withdrawal phase).

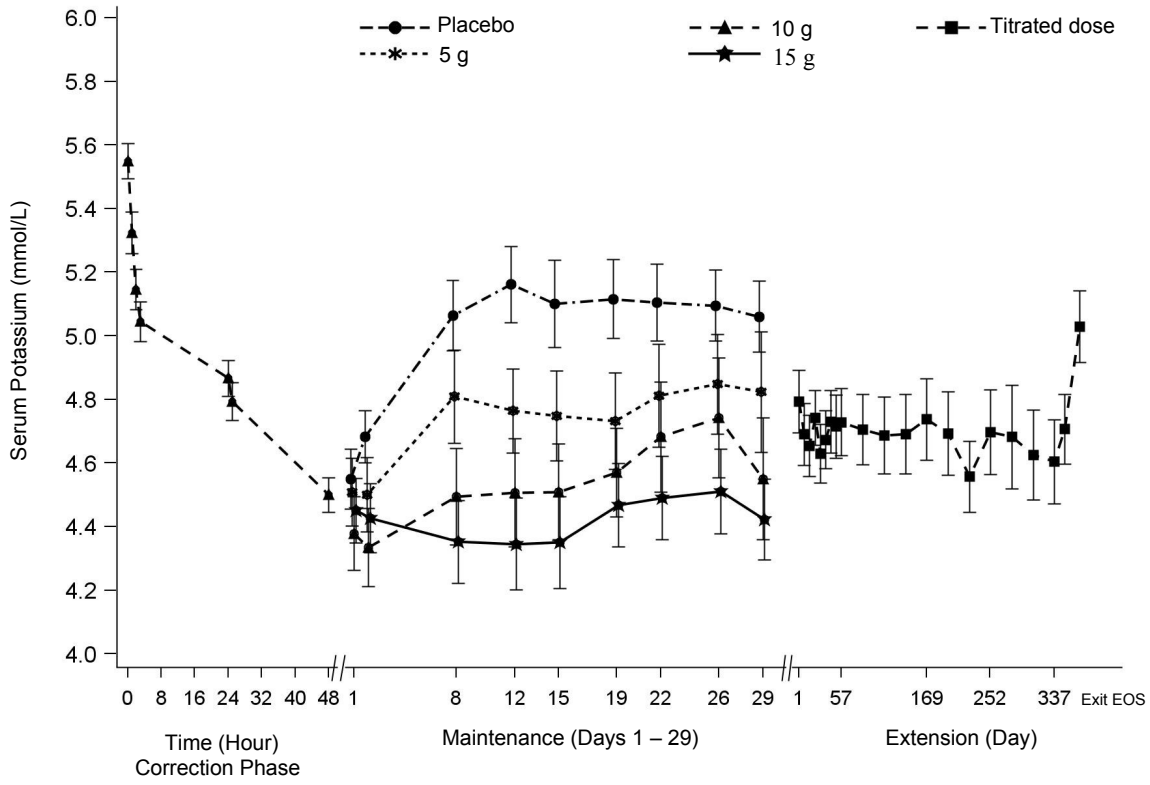
The proportion of subjects with average serum potassium < 5.1 mmol/L from Study Day 8 to 29 (three-week period) was greater at the 5 g, 10 g and 15 g once daily doses of Lokelma (80%, 90% and 94%, respectively), compared with placebo (46%). There was a mean decrease in serum potassium of -0.77 mmol/L, -1.10 mmol/L, -1.19 mmol/L and -0.44 mmol/L, respectively and the proportion of subjects who remained normokalaemic was 71%, 76%, 85% and 48% of subjects in the 5 g, 10 g, 15 g once daily doses of Lokelma and placebo groups, respectively.

Extend maintenance phase with Lokelma titration (open-label) results: 123 patients entered the 11-month open-label phase. The proportion of subjects with average serum potassium < 5.1 mmol/L was 88%, the average serum potassium level was 4.66 mmol/L and the proportion of serum potassium measurements below 3.5 mmol/L was less than 1%; between 3.5 and 5.1 mmol/L was 77%; or between 3.5 and 5.5 mmol/L was 93%, irrespective of other factors that might influence the serum potassium. Treatment was discontinued on study exit (Day 365).

Kaplan-Meier estimates of time to relapse for maintenance phase showed dose dependence in time to relapse with median time for 5 g dose ranging from 4 to 21 days depending on the baseline serum potassium values. Serum potassium should be monitored periodically and the Lokelma dose titrated as described in section 4.2 Posology and Method of Administration.

Figure 1 illustrates the mean serum potassium levels over the correction, maintenance and extension phases of the study.

Figure 1. Correction, maintenance and extension phases (Study 2): mean serum potassium levels



Study 3

A study in chronic kidney disease patients with hyperkalaemia

This study was a double-blind placebo-controlled dose-escalating study in 90 patients (60 Lokelma patients; 30 controls) with chronic kidney disease (defined as eGFR between 30 - 60 ml/min/1.73 m^2) and hyperkalaemia (baseline serum potassium 5.2 mmol/L, range

4.6 - 6 mmol/L). Patients were randomised to receive escalating doses of Lokelma (0.3 g, 3 g, and 10 g) or placebo, administered three times a day with meals for two to four days. The primary endpoint was the rate of change in serum potassium from baseline throughout the initial 2 days of treatment. The trial met the primary efficacy endpoint at the 3 g and 10 g doses of Lokelma compared to placebo. Lokelma at the 10 g dose and the 3 g dose resulted in mean maximal reductions of 0.92 mmol/L and 0.43 mmol/L, respectively. Twenty-four hour urine collections showed that Lokelma decreased urinary potassium excretion from baseline; -15.8 mmol/24 h compared to placebo +8.9 mmol/24 h ($p < 0.001$). Sodium excretion was unchanged relative to placebo (10 g, +25.4 mmol/24 h compared to placebo +36.9 mmol/24 h (NS)).

Study 4
An ongoing open-label maintenance study
In an open-label maintenance study to investigate the long term (up to 12 months) safety and efficacy of Lokelma in patients with hyperkalaemia, patients were dosed with 5 g once daily and could be titrated up to 15 g once daily or down to 5 g once every other day to maintain normokalaemia. The proportions of patients whose mean serum potassium was < 5.1 mmol/L and < 5.5 mmol/L over Months 3 to 12 was 89.0% and 98.8%, respectively.

Paediatric population
The European Medicines Agency has deferred the obligation to submit the results of studies with Lokelma in one or more subsets of the paediatric population in male and female children from birth to less than 18 years of age, with hyperkalaemia (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption
Sodium zirconium cyclosilicate is an inorganic, insoluble compound that is not subject to enzymatic metabolism. In addition, clinical studies have shown it not to be systemically absorbed. An *in vivo* mass balance study in rats showed that sodium zirconium cyclosilicate was recovered in the faeces with no evidence of systemic absorption. Due to these factors and its insolubility, no *in vivo* or *in vitro* studies have been performed to examine its effect on cytochrome P450 (CYP450) enzymes or transporter activity.

Elimination
Sodium zirconium cyclosilicate is eliminated via the faeces.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

5 or 10 g of powder in sachets of a PET/LDPE/LLDPE/aluminium foil laminate

Pack sizes: 3 or 30 sachets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1173/001
EU/1/17/1173/002
EU/1/17/1173/003
EU/1/17/1173/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

AstraZeneca AB
Gärtunavägen
SE-151 85 Södertälje
Sweden

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lokelma 5 g powder for oral suspension
sodium zirconium cyclosilicate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 5 g of sodium zirconium cyclosilicate.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for oral suspension.
3 sachets
30 sachets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1173/001 3 sachets
EU/1/17/1173/002 30 sachets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

lokelma 5 g

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lokelma 10 g powder for oral suspension
sodium zirconium cyclosilicate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each sachet contains 10 g of sodium zirconium cyclosilicate.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for oral suspension.
3 sachets
30 sachets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

AstraZeneca AB
SE-151 85 Södertälje
Sweden

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1173/003 3 sachets
EU/1/17/1173/004 30 sachets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

lokelma 10 g

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SACHET

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Lokelma 5 g powder for oral suspension
sodium zirconium cyclosilicate
Oral use

2. METHOD OF ADMINISTRATION

To open, cut across top.
Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Each sachet contains 5 g.

6. OTHER

AstraZeneca

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SACHET

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Lokelma 10 g powder for oral suspension
sodium zirconium cyclosilicate
Oral use

2. METHOD OF ADMINISTRATION

To open, cut across top.
Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Each sachet contains 10 g.

6. OTHER

AstraZeneca

B. PACKAGE LEAFLET

Package Leaflet: Information for the patient

Lokelma 5 g powder for oral suspension
Lokelma 10 g powder for oral suspension
sodium zirconium cyclosilicate

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Lokelma is and what it is used for

Lokelma contains the active substance sodium zirconium cyclosilicate.

Lokelma is used to treat hyperkalaemia in adults. Hyperkalaemia means that there is a high level of potassium in the blood.

Lokelma lowers the high levels of potassium in your body and helps to keep it at a normal level. As Lokelma passes through your stomach and gut it attaches to potassium and the two are carried together out of the body in your stools, lowering the amount of potassium in the body.

2. What you need to know before you take Lokelma

Do not take Lokelma
- If you are allergic to the active substance.

Warnings and precautions
Monitoring
Your doctor or nurse will check your blood potassium level when you start taking this medicine:
- This is to make sure you are getting the correct dose. The dose may be raised or lowered based on your blood potassium level.
- Treatment may be stopped if your blood potassium level becomes too low.

While you are taking Lokelma, tell your doctor or nurse if
- you need to have an X-ray, as Lokelma may affect the interpretation of the results.
- you have sudden or severe pain in your abdomen as this may be a sign of a problem that is

observed with other medications that work in the gastrointestinal tract.

Children and adolescents
Do not give this medicine to children and adolescents under 18 years of age. This is because the effects of Lokelma in children and adolescents are not known.

Other medicines and Lokelma
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.

In particular, tell them about any medicines which can change your blood potassium levels because your dose of Lokelma may need to be changed. These include:
- diuretics (medicines that increase urine production)
- angiotensin converting enzyme (ACE) inhibitors such as enalapril, and angiotensin receptor blockers which name ends with sartan (medicines for high blood pressure and for heart problems)
- renin inhibitors such as aliskiren (for high blood pressure)

If any of the above apply to you (or you are not sure), tell your doctor, pharmacist or nurse before taking this medicine.

Pregnancy and breast feeding
Pregnancy
Do not use this medicine during pregnancy because there is no information on its use in pregnancy.

Breast-feeding
No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to Lokelma is negligible. Lokelma can be used during breast-feeding.

Driving and using machines
This medicine has no or negligible influence on your ability to drive or to use machines.

3. How to take Lokelma

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How much to take
Starting dose - to lower your high potassium level to normal:
- The recommended dose is 10 g taken three times a day.
- The medicine takes one to two days to work.
- Do not take this starting dose for more than three days.

Maintenance dose - to keep your potassium level within the normal range after it has been lowered:
- The recommended dose is 5 g taken once a day.
- Your doctor may decide that you need more (10 g once a day) or less than this (5 g every other day).
- Do not take a maintenance dose of more than 10 g once a day.

Taking this medicine
- Try to take Lokelma at the same time each day.
- You can take this medicine with or without meal.

How to take

- Open the sachet and pour the powder into a drinking glass with approximately 45 ml of still (non-carbonated) water.
- Stir well and drink the tasteless liquid straight away.
- The powder does not dissolve and the liquid appears cloudy. The white powder will settle in the glass quickly. If this happens, stir the liquid again and drink it all up.
- Rinse the glass with more water and drink it all up to take all the medicine.

If you take more Lokelma than you should:
If you take more of this medicine than you should, talk to a doctor straight away. Do not take any more until you have spoken to a doctor.

If you forget to take Lokelma
- If you forget to take a dose of this medicine, skip the missed dose.
- Then take the next dose as usual at your normal time.
- Do not take a double dose to make up for a forgotten dose.

If you stop taking Lokelma
Do not reduce the dose of this medicine or stop taking it without talking to the doctor who prescribed it. This is because you may get high potassium levels in your blood again.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor or nurse if you experience any of the following:
Common side effects (may affect up to 1 in 10 people).
- you start to feel tired, or have muscle weakness or cramps, this may be a sign that your blood potassium has become too low. Talk to your doctor immediately if these symptoms become severe.
- you start to have a build up of fluid in the tissues, leading to swelling anywhere in your body (usually in the feet and ankles).

Not known (frequency cannot be estimated from the available data).
- you start to have abdominal pain or discomfort, nausea, vomiting, diarrhoea or constipation.
- you start to have itching of the skin or recognise redness or scaling of your skin.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Lokelma

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the sachet after 'EXP'. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Lokelma contains
The active substance is sodium zirconium cyclosilicate.
Lokelma 5 g powder for oral suspension
Each sachet contains 5 g of sodium zirconium cyclosilicate.
Lokelma 10 g powder for oral suspension
Each sachet contains 10 g of sodium zirconium cyclosilicate.

There are no other ingredients in this medicine.

What Lokelma looks like and contents of the pack
The powder for oral suspension is a white, free flowing powder, essentially free of debris and particulates. It comes in a sachet.

Lokelma 5 g powder for oral suspension
Each sachet contains 5 g of powder.

Lokelma 10 g powder for oral suspension
Each sachet contains 10 g of powder.

The sachets are supplied in a carton containing 3 or 30 sachets.

Marketing Authorisation Holder

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Manufacturer

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Other sources of information

Detailed information on this medicine is also available on the European Medicines Agency web site: http://www.ema.europa.eu.